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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/784,073	09/23/91	ANSON D	804-8

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EXAMINER	
WALSH, S	

ART UNIT	PAPER NUMBER
1814	33

DATE MAILED: 11/13/91

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 9-23-91 and 10-10-91 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ ~~days~~ from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 29-32 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 29-32 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☑ The ~~corrected or substitute~~ formal drawings have been received on 3-13-86. Under 37 C.F.R. 1.84 these drawings are ☑ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☑ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified ~~copy has~~ copies have ☑ been received ☐ not been received ☑ been filed in parent application, serial no. 06/839,215; filed on 5-14-86.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1814.

2. The preliminary amendment filed 23 September 1991 and the amendment filed 10 October 1991 have been entered.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-32 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to essentially full sequence factor IX protein. See M.P.E.P. §§ 706.03(n) and 706.03(z). The specification does not identify features which render a protein sufficiently similar to factor IX such that 90% activity level will be maintained. The specification does not provide guidance or direction that would enable the person of ordinary skill in the art to produce the range of species claimed.

4. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

4a. Claims 29-32 are rejected under 35 U.S.C. § 103 as being unpatentable over Suomela et al. or Osterud et al., in view of Schwinn. The factor IX protein claimed by Applicant was known in the art although the method used to produce the protein is not the same as those shown in the prior art. Note M.P.E.P. 706.03(e). Osterud et al. isolate and purify biologically active human factor IX, see Table 1. Suomela et al. teach production of highly purified biologically active human factor IX. In each of the references, human factor IX in substantially purified form is disclosed. The factor IX claimed by Applicant is inherently the same protein. While both Suomela et al. and Osterud et al. make clear that the purpose of their purification of factor IX is to provide factor IX preparations which can be used to treat factor IX deficiencies, neither reference teaches the explicit

preparation and administration of pharmaceutically acceptable formulations of factor IX. Schwinn teaches how to sterilize and prepare biologically active factor IX for infusion into human patients having factor IX deficiency, columns 3-4. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to use the methods of Schwinn et al. to treat patients with the preparations of Suomela et al. or of Osterud et al. because the advantages of highly purified biologically active factor IX were known at the time.

4b. Claims 29-32 are rejected under 35 U.S.C. § 103 as being unpatentable over Davie et al., in view of Wood et al., Nature 312:342-347, 22 November 1984, and further in view of Schwinn. Davie et al. teach a single isolated sequence of DNA encoding a monomorphic human factor IX, columns 3-6. Davie et al. teach that the DNA provides a continuous sequence coding for the factor IX, column 2 lines 12-15, and may be used for expression of polypeptides, column 1 lines 62-64. Davie et al. do not teach the expression of biologically active human factor IX. Wood et al. teach the expression of biologically active human factor VIII in cultured hamster kidney cell lines, see Abstract and page 335, 2nd column. Wood et al. teach that non-recombinant blood products used for pharmaceutical products are associated with complications caused by protein precipitates as well as the possible contamination by agents such as hepatitis virus and the

agent responsible for AIDS, page 331, paragraph bridging columns 1 and 2. Wood et al. provide motivation to produce recombinant blood products and use them in pharmaceutical products. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to insert the cDNA sequence of Davie et al. into the hamster kidney cell line of Wood et al. because Wood et al. teach the advantage of recombinantly produced blood products. Although both factor VII and IX proteins are coagulation cascade proteins, factor IX undergoes post-translational modifications distinct from the post-translational modifications of factor VIII. However, the factor IX produced by the hamster cells would inherently produce biologically active factor IX. Davie and Wood et al. do not teach a method of treating a human patient. Schwinn teaches how to sterilize and prepare biologically active factor IX for infusion into human patients having factor IX deficiency, columns 3-4. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to use the procedures of Schwinn et al. to administer the factor IX recombinantly produced from the cDNA of Davie et al. in the cells of Wood et al.

5. Applicants' Remarks filed 10 October 1991 have been considered but are not persuasive.

Applicants describe the instantly claimed protein as monomorphic, page 3 ¶3, but the claim language does not clearly

define such a limitation because each claim embraces a variety of undisclosed proteins. Applicants' arguments directed to the polymorphism-free factor IX are not persuasive for several reasons. First, Applicants have pointed out, in the paper dated Dec. 22, 1988, that factor IX may have ala or thr at position 148. However, no material difference between the two forms has been argued for, and as the two amino acids in question are members of a group recognized in the art to conservatively substitute for one another, see for example Schulz and Schirmer, Principles of Protein Structure at page 14 ¶6, it appears that no difference in function should be expected. Second, because it appears that the two forms function equivalently, it is not clear why either one used separately should be considered materially distinguished from the other or from a mixture of the two, or from the proteins of the references.

The three executed Declarations submitted with the response of December 22, 1988 have been considered. As noted by a previous Examiner during the prosecution of a parent application, the Declarations were considered to establish the non-obviousness of Applicants' process of producing factor IX over the prior art of record, but they do not show that the biologically active factor IX produced by this method is materially different from purified biologically active factor IX produced by other methods. Wood et al. is now made of record. The Examiner recognizes that no other plasma constituents would be present in the factor IX of

the invention. However, either Suomela et al., or Osterud et al., in combination with Schwinn is considered to render obvious a highly purified biologically active factor IX product, prepared by any method, and a method of treatment using the highly purified factor, because the combination of these references teaches the desirability of eliminating all contaminants from the preparation to be used in treatment. Davie et al. and Wood et al., in view of Schwinn, are considered to render obvious a highly purified biologically active monomorphic factor IX product, prepared by recombinant means, and a method of treatment using the recombinant factor, because the combination of these references teaches recombinant production and the desirability of eliminating plasma contaminants and viruses from the preparation to be used in treatment.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Walsh whose telephone number is (703) 308-2957.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

S. Walsh SW
November 6, 1991

ROBERT A. WAX
SUPERVISORY PATENT EXAMINER
ART UNIT 1814